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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,265	09/05/2001	Keiko Yamasaki	2001-1026A	3583

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EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/914,265	YAMASAKI ET AL.	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2004* .

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The receipt is acknowledged of applicants' request for extension of time and amendment, both filed 05/20/2004.

Claims 10-12 have been added. Claims 7-12 are included in the prosecution.

Claim Rejections - 35 USC § 103

1. Claims 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,562,363 ('363) in view of US 5,725,874 ('874).

US '363 teaches a composition for topical application to the skin comprising two or more active agents to achieve therapeutic effect or multiple therapeutic effects or both (abstract; col.2, lines 53-60; col.7, lines 57-59; col.8, lines 24-26). Non-steroidal anti-inflammatory agent can be administered in conjunction with a local anesthetic agent to provide reduction in pain by means of both the analgesic effect and the anesthetic effect of such agents (col.8, lines 26-31). Analgesics include bufexamac, felbinac, flurbiprofen, indomethacin, ketoprofen, and suprofen (col.10, lines 5-34). Anesthetics include benzocaine, dibucaine, lidocaine, procaine, and tetracaine (col.10, line 45 till col.11, line 3; col.30, lines 22-26). The concentration of the active agents can be varied independently from 1-40% of the total weight of the composition in order to achieve the desired therapeutic effect (col.32, lines 45-48, 60-62). The composition further

comprising water-soluble polymer, cross-linking agent, water, and polyhydric alcohol (col.2, lines 47-51; col.3, lines 17, 47, 59; col.5, lines 41-44; col.7, lines 38-40). The composition included in a delivery device as reservoir that has a backing layer (col. 3, lines 39-41; col.41, lines 13-25).

Although the reference disclosed the generic teaching of including a cross-linking agent in the composition, the reference does not teach specifically the aluminum compounds as the cross-linking agent.

US '874 teaches a percutaneous preparation that has long stability, releasability, percutaneous absorbability and safety for the skin (col.3, lines 40-43). The preparation comprising 0.01 to 20% of a drug; water-soluble polymer; water; humectants selected from polyhydric alcohol including polyethylene glycol, propylene glycol, butylenes glycol, glycerol, and sorbitol; and cross linking agents such as aluminum compounds (abstract; col.3, lines 28-30, 66-67; col.4, lines 1-2, 8-10, 14-20). The dosage form of the preparation can be in the form of reserve patches that have a support (abstract; col.3, line 37; col.4, line 47). The drug to be delivered in the percutaneous preparation includes anti-inflammatory agents selected from diclofenac, ketoprofen, flurbiprofen, felbinac, and indomethacin; and local anesthetic such as lidocaine, benzocaine, and procaine (col.2, lines 60-63; col.3, lines 11-12; col.4, line 66 till col.5, line 2).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to deliver the transdermal patch comprising combination of analgesic and local anesthetic in the composition that comprises cross-linking agent as disclosed by US '363, and replace the cross-linking agent by the aluminum compounds

as disclosed by US '874, motivated by the teaching of US '874 that the percutaneous preparation that has the aluminum compounds has long stability, releasability, percutaneous absorbability and safety for the skin, with reasonable expectation of having a stable percutaneous composition that relieves pain for prolonged period of time.

Response to Arguments

Applicant's arguments filed 05/20/2004 have been fully considered but they are not persuasive. Applicants traverse the above rejection by arguing that US '363 does not teach the between 20-60%. US '874 teaches nothing about a composition comprising a polyvinylpmolidone polymer as described in US '363. Thus, there is no motivation to apply the combination of drugs described in US '363 to the preparations disclosed in US '874 to arrive at the claimed invention of an external skin patch which comprises, among other ingredients, 20 to 60% by weight of water based upon the total weight of the adhesive gel base with an expectation of achieving a superior pain relief effect.

In response to the above argument, the examiner position is the claims are directed to composition, and all the element of the compositions are taught by US '363, except for the specific crosslinking agent. US '874 is relied upon for the solely teaching of the aluminum compounds as crosslinking agent. The primary reference recognized the combination of analgesic and anesthetic as effective treatment for pain. It would have been obvious to one having ordinary skill in the ad at the time the invention was

made to adjust the amount of water, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable / ranges involves only routine skill in the art. *In re Aller* 105 USPQ 233. The specification disclosed 10-80% of water in the composition, and the prior art disclosed less than 10%, and that can be 9.99%. the burden is shifted to applicant to show difference between 9.99% and 10%. No criticality has been shown in the specific amount of water. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, and because the secondary reference was relied upon for the crosslinking agent, one having ordinary skill in the art would have been used aluminum compounds as crosslinking agent motivated by the teaching of US '874 that the percutaneous preparation that has the aluminum compounds has long stability, releasability, percutaneous absorbability and safety for the skin, with reasonable expectation of having a stable percutaneous composition that relieves pain for prolonged period of time.

2. Claims 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,686,112 ('112) in view of US '874.

US '112 disclosed a transdermal therapeutic system for topical application of systemically acting pharmaceutical substances (abstract). To improve efficacy and tolerability of a transdermal systemic pain or rheumatism treatment, analgesics and local anesthetics are delivered in single dosage topical pharmaceutical form including non-steroidal anti-inflammatory analgesics such as indomethacin and diclofenac, and local anesthetics such as lidocaine and benzocaine (col.3, lines 1-9; col.6, lines 16-18).

The reference does not teach a specific preparation for the transdermal therapeutic system and doses of the drugs as disclosed by applicants.

US '874 teaches a percutaneous preparation that has long stability, releasability, percutaneous absorbability and safety for the skin (col.3, lines 40-43). The preparation comprising 0.01 to 20% of a drug; water-soluble polymer; water; humectants selected from polyhydric alcohol including polyethylene glycol, propylene glycol, butylenes glycol, glycerol, and sorbitol; and cross linking agents such as aluminum compounds (abstract; col.3, lines 28-30, 66-67; col.4, lines 1-2, 8-10, 14-20). The dosage form of the preparation can be in the form of reserve patches that have a support (abstract; col.3, line 37; col.4, line 47). The drug to be delivered in the percutaneous preparation includes anti-inflammatory agents selected from diclofenac, ketoprofen, flurbiprofen, felbinac, and indomethacin; and local anesthetic such as lidocaine, benzocaine, and procaine (col.2, lines 60-63; col.3, lines 11-12; col.4, line 66 till col.5, line 2).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to deliver the transdermal patch comprising combination of analgesic and local anesthetic to relief pain as disclosed by US '112, and deliver the

combination of the drugs in the percutaneous preparation disclosed by US '874, motivated by the of any of US '874 that the percutaneous preparation that has water-soluble polymer, water, humectants and cross-linking agent has long stability, releasability, percutaneous absorbability and safety for the skin, with reasonable expectation of having a stable percutaneous composition that relieves pain for prolonged period of time.

Response to Arguments

Applicant's arguments filed 05/20/2004 have been fully considered but they are not persuasive.

Applicants traverse the above rejection by arguing that US '112 does not disclose the specific combination of a local anesthetic and a nonsteroidal antiphlogistic analgesic agent. The Examiner appears to rely on the position that it is prima facie obvious to combine two compositions each of which is known to be useful for the same purpose, such as analgesics and anesthetics, both for relief of pain. However, even if arbitrarily selecting any two compositions each of which is useful for relief of pain, the remarkable effect of the present invention cannot be expected. Applicants intend to establish the nonobviousness and patentability of the claimed invention by demonstrating that the claimed invention possesses an unexpected synergistic effect in comparison to administration of a random combination of anesthetic or analgesic taught in the prior art. There is not motivation to combine the references.

In response to the above arguments, the examiner position is that US '112 teaches the mixture of analgesic and anesthetic. US '874 teaches the structure of the patch as claimed by applicant. The rationale to modify or combine the prior art does not have to be expressly stated in the prior art; the rationale may be expressly or impliedly contained in the prior art or it may be reasoned from knowledge generally available to one of ordinary skill in the art and the reason to modify the reference may often suggest what the applicant has done. In response to applicant's argument that there is no suggestion to modify or combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one having ordinary skill in the art at the time of the invention to deliver the transdermal patch comprising combination of analgesic and local anesthetic to relief pain as disclosed by US '112, and deliver the combination of the drugs in the percutaneous preparation disclosed by US '874, motivated by the of any of US '874 that the percutaneous preparation that has water-soluble polymer, water, humectants and cross-linking agent has long stability, releasability, percutaneous absorbability and safety for the skin, with reasonable expectation of having a stable percutaneous composition that relieves pain for prolonged period of time.

Response to Amendment

3. The declaration under 37 CFR 1.132 filed 05/20/2004 is insufficient to overcome the rejection of claims 7-12 based upon obviousness rejection under USC 103 (a) over US '363 in view of US 874 and US 112 in view of US '874 as set forth in the last Office action because: it include(s) statements which amount to an affirmation that the claimed subject matter functions as it was intended to function. This is not relevant to the issue of nonobviousness of the claimed subject matter and provides no objective evidence thereof. See MPEP § 716. The experiments show comparison between the composition of the instant invention that comprises combination of analgesic and anesthetic and composition comprises analgesics only, but do not show comparison between the instant composition and composition comprises anesthetic alone in order to have complete comparative data. No statistical evaluation to determine the if there is any additive or synergistic effects of both elements of the composition. Furthermore, the evaluation is subjective based on individual judgment that can be controlled by many factors, such as individual pain tolerance threshold, individual condition to be treated, etc. The score of 1-4 does not show what is the difference between complete remission and effective.

In view of the foregoing, when all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

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